REMARKS

Claims 1-7, 9-10, 12, 14, 16-21, 23-26, 28-34, 44-49, 51-52, 54-60, 62-63, 65-66, and 68-75 are presented for examination.

Claims 1, 9, 12, 14, 23-24, 28, 51-52, 54-55, 62 and 65-66 are currently amended.

Claims 8, 11, 13, 15, 22, 27, 35-43, 50, 53, 61, 64, 67 and 76-128 are canceled without disclaimer or prejudice.

Claims 2-7, 10, 16-21, 25-26, 29-34, 44-49, 56-60, 63 and 68-75 are pending as originally filed.

Claims 1 and 28 are amended to incorporate the limitations of original Claims 8, 11, 13 and 15. Accordingly, Claims 8, 11, 13, and 15 are canceled. Similarly, Claim 54 is amended to incorporate the limitations of original Claims 61, 64 and 67. Accordingly, Claims 61, 64, and 67 are canceled. Claim 54 is also amended to delete the allegedly redundant phrase "comprising a programmable pump" in part (b), as required by the Office Action. Claims 14, 23-24, 51-52, 62 and 65-66 are amended to recite correct dependency in light of the canceled claims. Claim 55 is amended to correct a minor grammatical error. The amendments to the claims are supported by the claims as originally filed. No new matter is contained in the amendments. Entry is respectfully requested.

Claim Objections

The Office Action objected to Claims 23-24 and 51-52 for depending on previously canceled claims, the subject matter of the canceled claims having been incorporated into the

corresponding independent claim. The appropriate corrections are made by the present amendment.

The Office Action also objected to Claim 54 for duplicating elements of the programmable pump that were previously recited in part (b). The present amendment deletes the phrase "comprising a programmable pump" in part (b). Thus, the system claim recites a catheter system element that is described as delivering the therapeutic protein formulation at a programmed delivery rate. The following "wherein" clause is no longer duplicative, because this clause modifies part (b), indicating that the pump element of part (c) provides for the programmable delivery rate that is then delivered by the catheter system element.

Rejection under 35 U.S.C. § 103(a)

The Office Action rejected Claims 1-6, 8-12, 18-21, 23-26, 28-33, 45-49, 51-52, 54-59, 61-65, and 69-75 as being unpatentable over U.S. 5,814,014 (Elsberry *et al.*) in view of U.S. 5,433,946 (Allen *et al.*). The Office Action alleged that Elsberry *et al.* teaches the limitations of Claim 1 except for a therapeutic protein formulation that has been modified for enhanced cellular uptake properties. The Office Action relied upon Allen *et al.* for the use of a therapeutic protein formulation that has been modified for enhanced cellular uptake properties.

However, the *prima facie* case of obviousness is not established over the presently pending independent Claims 1, 28 and 54, because neither Elsberry *et al.* nor Allen *et al.* teaches a linker being a streptavidin-biotin complex. Likewise, the rejected dependent Claims 2-6, 9- 10, 12, 18-21, 23-26, 29-33, 45-49, 51-52, 55-59, 62-63, 65, and 69-75 are unobvious over the cited

references, because *prima facie* obviousness has not been established as to their independent base claims.

The Office Action rejected Claims 7, 16-17, 34, 44, 60, and 68 as being unpatentable over Elsberry *et al.* as modified by Allen *et al.* and further in view of U.S. 6,015,572 (Lin *et al.*). For the reasons set forth above, the system of base Claims 1, 28, and 54 are not taught by Elsberry *et al.* as modified by Allen *et al.* Therefore, the inclusion of Lin *et al.* for the recitation of GDNF and FMRP proteins and the pH maintaining elements recited in Claims 7, 16-17, 34, 44, 60, and 68 does not establish *prima facie* obviousness, because these proteins are modified as set forth in the independent claims in a manner that is not taught or suggested by the cited references.

The Office Action rejected Claims 13-15 and 66-67 as being unpatentable over Elsberry *et al.* as modified by Allen *et al.* and further in view of U.S. 2003/0129186 (Beliveau *et al.*), which allegedly teaches a linker being a streptavidin-biotin complex (¶ 189). However, Beliveau *et al.* does not teach a streptavidin-biotin complex as a linker between a therapeutic protein and a transport aid. Instead, the reference teaches the complex being a label for detecting a signal wherein biotin is covalently bound to a molecule, which is then bound to another molecule (e.g., streptavidin), which is either inherently detectable or covalently bound to a signal system, such as a detectable enzyme, a fluorescent compound, or a chemiluminescent compound. Thus, the streptavidin-biotin complex is used for detection, and not as the claimed linker for the purpose of facilitating blood-barrier transport. One skilled in the art would not be motivated to use this

label element of Beliveau *et al.* to enhance transport of the therapeutic formulations of Elsberry *et al.* or Allen *et al.*, and such a combination would not lead to formulation of the claimed invention.

Non-statutory obviousness-type double patenting rejection

The Office Action rejected claims 1-2, 4, 28-9, 31, 54-55, and 57 on the ground of non-statutory obviousness-type double patenting over Claim 1 of U.S. 5,814,014 (Elsberry *et al.*). The Office Action alleged that the conflicting claims are patentably indistinct, because the claim requires the structural features of the instant application, which are a pump, a catheter capable of delivering a therapeutic dosage, a sensor for generating a signal related to an attribute of the CNS, and control means responsive to the signal generated. However, Claim 1 of the prior patent does not require the streptavidin-biotin complex used as a linker between the therapeutic protein formulation and the transport aid. Accordingly, the present invention is patentably distinct from the prior patent.

The Office Action also rejected Claims 1-2, 4, 24, 28-29, 31, 52, 54-55, 57, and 74 on the ground of non-statutory obviousness-type double patenting over Claims 1, 3 and 11 of U.S. 6,056,725 (Elsberry). The Office Action alleged that the similar structures are recited for treating Alzheimer's disease: a pump, a source of indomethacin, a catheter connected to a pump into the hippocampus or lateral ventricle, and the pump adapted for subcutaneous placement. This prior patent also does not require the streptavidin-biotin complex used as a linker between the therapeutic protein formulation and the transport aid. Accordingly, the present invention is

patentably distinct from the prior patent.

Respectfully submitted,
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